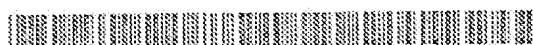


(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
7 August 2003 (07.08.2003)

PCT

(10) International Publication Number  
**WO 03/064502 A1**

(51) International Patent Classification: C08G 83/00, 85/00

(21) International Application Number: PCT/FI03/00074

(22) International Filing Date: 30 January 2003 (30.01.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 20020186 31 January 2002 (31.01.2002) FI

(71) Applicant and

(72) Inventor: RISSANEN, Kari [FI/FI]; Hankamäentie 13, FIN-41520 Hankasalmi (FI).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ROPPONEN, Jarmo [FI/FI]; Taitoniekantie 15 C 28, FIN-40740 Jyväskylä (FI); NÄTTINEN, Kalle [FI/FI]; Vapaudenkatu 79 A 8, FIN-40100 Jyväskylä (FI).

(74) Agent: FORSSÉN &amp; SALOMAA OY; Esikinkatu 2, FIN-00100 Helsinki (FI).

(81) Designated States (national): AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK (utility model), SE, SI, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: POLYESTER DENDRIMERS, METHOD FOR THE MANUFACTURE THEREOF, AND THEIR USE

(57) Abstract: The invention is related to polyester dendrimers of a polyol with 2-64 reactive hydroxyl groups wherein ester functions are formed using alternating sequences of haloacetyl halide and alkali metal salt of a carboxylate. Said polyester dendrimers are prepared via a two step process from a polyol and a haloacetyl halide (step 1) and subsequent reaction with an alkali metal salt of a carboxylate (step 2). Further, the invention is directed to the use of said polyester dendrimers as cross linkers in polymers and gels, active components in glues and coatings, matrix material in inorganic or organic or bio-composites as well as ionselective complexation agents for analytical and catalysis applications.

WO 03/064502 A1

## Polyester dendrimers, method for the manufacture thereof, and their use

### 5 Background of the invention

#### Field of the invention

The invention is related to new polyester dendrimers prepared via a two-step  
10 process from a polyol and a haloacetyl halide (step 1) and subsequent reaction  
with an alkali metal enolate (step 2). Further, the invention is directed to the use  
of said dendrimers as cross linkers in polymers and gels, active components in  
glues and coatings, matrix material in inorganic or organic or bio-composites as  
well as ionselective complexation agents for analytical and catalysis applications.

15

#### State of the art

Chemically discrete, monodisperse and extremely branched, polymer-like tree-  
20 shaped macromolecules form a relatively new family of compounds, which has  
been studied very intensively over the last 10 years. These macromolecules pos-  
sess a spherical 3-D molecular structure and they are commonly called dendritic  
polymers, fractal molecules or nowadays dendrimers. The physical and chemical  
properties of dendrimers deviate greatly from the properties of conventional linear  
25 oligomers or polymers. Linear oligomers and polymers, which have sufficiently  
large molecular weight, usually over 1000 for practical applications, such as cur-  
able polyester resins, consist of a long molecular chain with a functional group  
residing at the end of it.

30 Dendrimers have a very compact spherical structure and their surface can contain  
from a few to hundreds of functional groups depending on the nature and size of  
the dendrimer. The unique physical and chemical properties of dendrimers, cou-

plied with specific functional groups, accomplish extremely interesting and applicable properties when compared with conventional linear polymers. The low intrinsic viscosity of dendrimers versus molecular weight and possibility to multifunctionality on the surface of the dendrimer are properties, which are either completely absent or very difficult to achieve with linear polymers.

Dendrimers according to the state of the art are manufactured using two principal methods, by an iterative process starting from a core molecule (so-called divergent method) or by processing first the branched parts (so-called dendrons) and joining these parts into a core molecule (so-called convergent method). Using either of said two methods, the shape, size and physical and chemical properties of the molecule can be varied as desired. Dendrimers with a very branched structure can be used in many applications, such as catalysts, parts of pharmaceuticals, carriers or transporters, imaging agents in medicine, in improving viscosity or general properties of cosmetics, as glues and coating agents, matrix material for inorganic or organic or bio-composites, lubricants, anti-corrosion agents, pesticides or agricultural chemicals and polyfunctional cross linkers in polymer production, medical and dentistry preparates, dentures and prosthesis.

Patent US 5,834,118 and publication WO 96/07688 disclose a group of dendritically hyperbranched methacrylated and acrylated polyesters, which have a variable amount of terminal double bond functions per molecule, and a method for producing thereof. Said publications disclose a process for producing a hyperbranched polyester consisting of a polyol core containing 3-10 reactive hydroxyl groups and an aromatic carboxylic acid anhydride with 2-4 carboxyl groups. In the first step, each of the hydroxyl groups of the polyol form an ester bond with one of the anhydride groups of the polycarbonyl anhydride. Thus formed hyperbranched polyester carboxyl functionalized molecule reacts in the second step with glycidyl (meth)acrylate or allylglucosyl ether and the remaining anhydride and carboxylic acid groups react forming ester bonds. In the last step, the free hydroxyl groups on the surface of the hyperbranched polyester are functionalized by

a reaction with ester bond forming methacrylic anhydride and/or aliphatic carboxylic acid anhydride. The hyperbranched polyesters prepared by this method are suitable for UV-radiation curable resin applications. Since this method lacks control in the second step i.e. the anhydride reaction, several products are formed resulting in a final product, hyperbranched polyester actually containing a mixture of products.

*Publications WO 93/17060, WO 96/12754, WO 96/13558 and WO 96/19537 disclose a process for producing hyperbranched polyesters and their use as radiation curable resins, lubricants, binders and in thermoset applications. Said process is a one-pot process where a suitably functionalized polycarboxylic acid is polymerized into a mixture of hyperbranched polyesters. Since the one-pot polymerization cannot be controlled, also this method results in a mixture of variable sized hyperbranched polyesters.*

Two commercially produced dendrimer families are currently available. Polypropylene imine dendrimer, sold under the tradename Astramol<sup>®</sup>, is produced using the divergent method from ethylenediamine which is reacted with acrylonitrile via Michael reaction. The formed polynitrile is catalytically reduced to an amine and, by repeating these two steps, polypropylene imine dendrimers having 4, 8, 16, 32 or 64 amino groups on the surface can be produced. The divergent method is also used for the production of Starburst<sup>®</sup> dendrimers. Ammonia as the core molecule is reacted with ethyl/methylacrylate via Michael reaction forming an amine ester, which is subsequently reacted with excess of ethylenediamine and a polyamidoamine dendrimer is formed having up to 64 amino groups on the surface. Neither of these commercially available dendrimers is a pure product but they contain mixtures of products. Further, none of the dendrimers according to the state of the art are pure single compounds but mixtures of compounds, and none of them are true crystalline compounds.

The specific physical and chemical properties and functionalities make dendrimers extremely interesting when new materials are designed and developed or when the properties of existing materials are being tuned and improved. Based on the above teachings it can be seen that there is an evident need for novel pure polyester dendrimers and methods for their production.

### Object of the invention

10 An object of the invention is to provide novel pure polyester dendrimers.

A further object of the invention is to provide novel pure polyester dendrimers with desired functionality.

15 A further object of the invention is a method for the manufacture of novel pure polyester dendrimers.

A further object of the invention is the use of said novel pure polyester dendrimers.

20

The characteristic features of the polyester dendrimers, of the method for the manufacture of said polyester dendrimers, and of the use of said polyester dendrimers are presented in the claims.

25

### Summary of the invention

The above stated objects can be achieved and the disadvantages of the products and methods of the state of the art can be avoided or at least significantly reduced using the solution according to the invention. The polyester dendrimers according to the invention are polyester dendrimers of a polyol with 2 - 64 reactive hydroxyl

30

groups, wherein the surface of the dendrimer is formed using an alternating sequence of haloacetyl halide and an alkali metal enolate.

## 5 Detailed description of the invention

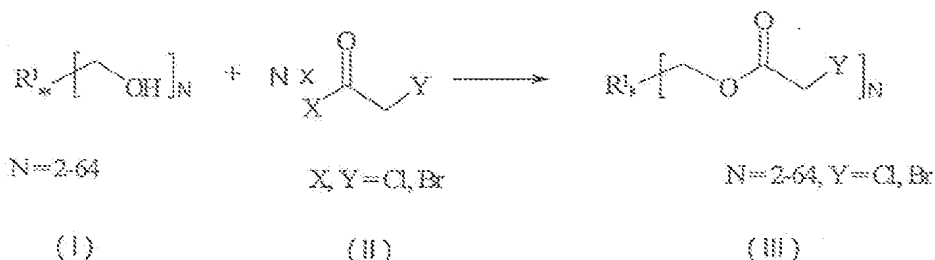
The polyester dendrimers according to the invention are polyester dendrimers of a polyol with 2 - 64 reactive hydroxyl groups wherein the surface of the dendrimer is formed using an alternating sequence of haloacetyl halide and an alkali metal enolate, and preferably said dendrimers are surface functionalized by bis- or tris-methyl and ethyl esters. The polyester dendrimers according to the invention are pure single crystal forming crystalline compounds or liquid compounds. The polyester dendrimers are manufactured by reacting a bisfunctionalized chemical, a haloacetyl halide, with a core molecule that contains hydroxyl groups, such as a polyol with 2 - 64 reactive hydroxyl groups. This reaction produces an easily separable reactive dendritic polyester polyhalide, which readily reacts subsequently with a third chemical, an alkali metal enolate, producing the desired polyester dendrimer.

20 By choosing the core molecule in such a way that the chemical reactions will produce ester bonds, a dendritic polyester structure can be obtained. According to the invention pure polyester dendrimers with the general formula (V) are produced for various applications with good chemical yield and from cheap and often easily available starting materials according to the following Scheme 1.

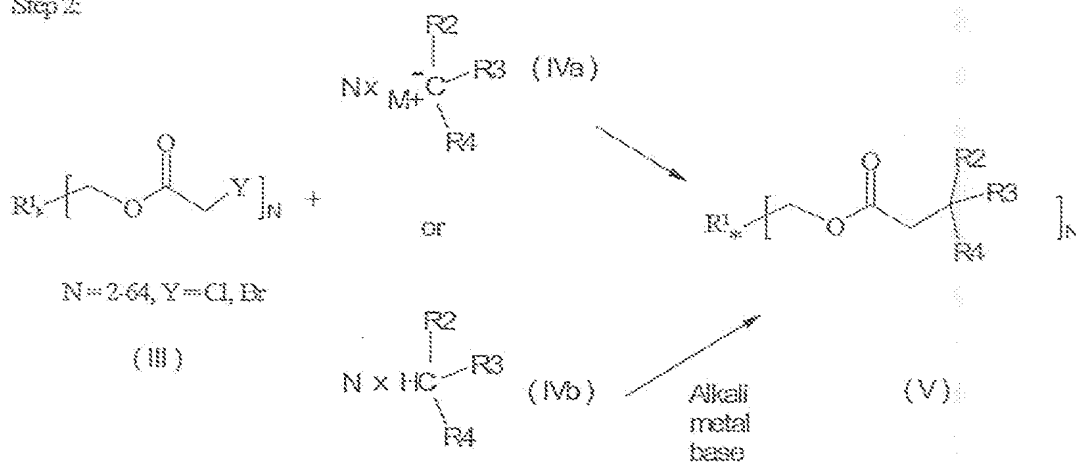
25

## SCHEME 1

Step 1:



Step 2:



In step 1, a polyol (I), where N is 2–64, is allowed to react with a haloacetyl halide (II) where X and Y are Cl or Br, which (II) also may act as a solvent. The reaction mixture is refluxed until the formation of hydrogen halide is ceased. Then, after optional recrystallization from a suitable solvent, a dendritic polyester polyhalide (III) is obtained. Alternative esterification methods are well known in the art and can be equally well utilized. These include the use of  $\alpha$ -haloacetyl anhydride or  $\alpha$ -haloacetic acid with some condensing agent, such as cyclohexylcarbodiimide. Currently haloacetyl halides are preferred.

10

In step 2 the obtained polyester polyhalide (III) is allowed to react with an alkali metal enolate (IVa), or bis- or tris(carbonyl)methane derivative (IVb) together

with an alkali metal base, in a solvent or a mixture of solvents and preferably at an elevated temperature. Then a suitable solvent is added to the reaction mixture, the reaction mixture is washed with water, with concentrated alkali metal hydrogen carbonate and again with water. The solvent layer is dried and the solvent is  
5 evaporated, preferably under vacuum. A suitable solvent is added to the viscous oily product and the obtained polyester dendrimer (V) crystallizes in the case it is a crystalline compound. In the case the products are not crystalline they are treated as above with the final step being removal of the solvent, preferably under vacuum.

10

Group  $R^1$  is an unsubstituted or substituted aliphatic group selected from the group consisting of linear or branched alkyl groups containing 1–100, preferably 1–20 and particularly preferably 1–10 carbon atoms, linear or branched alkenyl and alkynyl groups containing 2–100, preferably 2–20 and particularly preferably  
15 2–10 carbon atoms, or a (hetero) aromatic group selected from the group consisting of 1,n-dihydroxybenzene, where n is 2,3 or 4, 1,n,y-trihydroxybenzene, where n is 2,3 or 4 and y is 3,4,5 or 6, preferably 1,3,5-trihydroxybenzene. Optionally the aliphatic group is substituted with (hetero) aliphatic or (hetero) aromatic groups. Particularly preferably  $R^1$  is a methyl, ethyl, propyl, isobutyl or butyl  
20 group.

Groups  $R^2$ ,  $R^3$  and  $R^4$  are selected, independently from each other, so that a bis(carbonyl)methane or tris(carbonyl)methane derivative is obtained. This selection is done from a group consisting of H, COH, CSH, COOR<sup>5</sup>, COSR<sup>5</sup>, CSOR<sup>5</sup>,  
25 CSSR<sup>5</sup>, COR<sup>5</sup>, CSR<sup>5</sup>, CONR<sup>5</sup>R<sup>6</sup>, CSNR<sup>5</sup>R<sup>6</sup>. Preferable ones are methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and hexyloxycarbonyl groups and aryloxycarbonyl groups. Particularly preferable ones are methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and hexyloxycarbonyl groups.

30



Groups  $R^5$  and  $R^6$  are selected, independently from each other, from a group consisting of H, aliphatic groups, alkenyl groups, alkynyl groups, aryl groups, (hetero) aromatic groups and aliphatic heterocyclic groups, which contain oxygen, sulfur, nitrogen or phosphorous atoms. Suitable aliphatic groups are linear and  
5 branched alkyl groups containing 1–100, preferably 1–20 and particularly preferably 1–10 carbon atoms, linear and branched alkenyl or alkynyl groups containing 2–100, preferably 2–20 and particularly preferably 2–10 carbon atoms. Particularly preferable ones are methyl, ethyl, propyl and butyl groups. Optionally, the aliphatic group is also substituted with (hetero) aliphatic or (hetero) aromatic  
10 groups. An example of such a substituted aliphatic group is isobutyl group. Suitable aryl groups, (hetero) aromatic groups and aliphatic groups, which contain oxygen, sulfur, nitrogen or phosphorous atoms are 3-hydroxymethylpyridine, 2-hydroxymethylthiophene, 2-hydroxymethylfuran, 2-hydroxymethylpyrrole and hydroxymethyldiethyl phosphonate groups.

15

The starting material polyol (I) is preferably selected from diols, triols, tetrols or hexahydroxycyclohexanes, such as inositol and particularly preferably it is pentaerythritol or dipentaerythritol.

20 The starting material haloacetyl halide (II) is preferably chloroacetyl chloride, bromoacetyl bromide or bromoacetyl chloride.

The starting material alkali metal enolate is selected from alkali metal enolates of functionalized bis(carbonyl)methane or tris(carbonyl)methane compounds (IVa),  
25 or from functionalized bis(carbonyl)methane or tris(carbonyl)methane compounds (IVb) together with an alkali metal base wherein the desired alkali metal enolate is formed *in situ*. Particularly preferable ones are  $\text{NaC}(\text{CO}_2\text{Me})_3$ , and  $\text{H}_2\text{C}(\text{CO}_2\text{Me})_2$  together with  $\text{K}_2\text{CO}_3$ .

30 The method according to the invention is described in detail in the following. In step 1, 1–50 mol, preferably 1–5 mol of haloacetyl halide (II) (in excess) per hy-

- droxyl group is reacted with a polyol (I) with 2-64, preferably 2-20 and particularly preferably 3-12 hydroxyl groups, at a temperature of 20-150 °C, preferably at 60-150 °C, and the reaction mixture is refluxed until gaseous acid formation (hydrogen halide) is ceased. The excess of haloacetyl halide is removed by evaporation, preferably under vacuum and the solid intermediate (III) obtained is separated, preferably filtered and dried. Optionally the intermediate also can be recrystallized from a solvent or a mixture of solvents, such as alcohols, ketones and polar hydrocarbons, suitably from ethanol.
- 5 In step 2, the intermediate (III) obtained from step 1 is reacted with an alkali metal enolate (IVa), or bis- or tris(carbonyl)methane compound (IVb) together with an alkali metal base, in an inert aprotic solvent or a mixture of inert aprotic solvents, preferably DMF, at a temperature of 20-120 °C, preferably at 60-100 °C. The reaction mixture is then agitated at a temperature of 20-120 °C, preferably 80-100
- 10 °C, for approximately 20 hours and it is then cooled to room temperature. A non-polar solvent or a mixture of non-polar solvents, suitably chloroform, is added to the reaction mixture, and the obtained mixture is then washed with water, then with saturated alkaline earth metal hydrogen carbonate, dried and the solvent is evaporated, preferably under vacuum. A polar solvent or a mixture of polar sol-
- 15 vents, such as an alcohol like ethanol is added and the obtained final product dendrimer (V) is separated. In the case it is a crystalline product, it is preferable filtered and dried and if it is a liquid, it may be distilled under vacuum.

In general, when said process containing two steps is used, second generation

25 dendrimers are obtained.

The novel polyester dendrimers according to the invention have several advantages. The products are very pure, no or very little undesired side-products or mixtures of products are formed. This results in that the cureability of polyester products made from these dendrimers is good as no or very little impurities interfere in

30 the curing reaction.

Additionally, due to the unique and true crystalline structure and crystallinity of many of the products, and because of the reaction conditions, the obtained dendrimers contain no or very little detectable amounts of solvents. These polyester dendrimers, many of which are first truly crystalline polyester dendrimers, are  
5 easy to handle, they are stable for long storage periods and they are non-hygroscopic. Because said dendrimers are chemically polyesters, they also are at least partially biodegradable and relatively non-toxic.

The method according to the invention has several advantages. The yields are  
10 good, very pure final products can be obtained, the starting materials are cheap and usually commercially available substances, and almost all materials used in the process may be recirculated.

Further, the properties of the polyester dendrimer product can be varied by vary-  
15 ing the chain length and functionality of the R-groups.

The polyester dendrimers according to the invention may be used in many applications, such as catalysts, parts of pharmaceuticals, carriers, transporters, imaging agents in medicine, in improving viscosity or general properties of cosmetics, as  
20 glues and coating agents, matrix material for inorganic or organic or bio-composites, lubricants, anti-corrosion agents, pesticides or agricultural chemicals and polyfunctional cross linkers in polymer and gel production, medical and dentistry preparates, dentures and prosthesis as well as ionselective complexation agents for analytical and catalysis applications, like the commercially available  
25 dendrimers are used. It is evident that the polyester dendrimers according to the invention can be used in similar application fields as what is disclosed in US 5,834,118, WO 96/07688, WO 93/17060, WO 96/12754, WO 96/13558 and WO 96/19537 for dendrimers according to the state of the art.

30 The invention is illustrated by means of the following examples. It is clear for a man skilled in the art that the invention is not meant to be limited solely to these

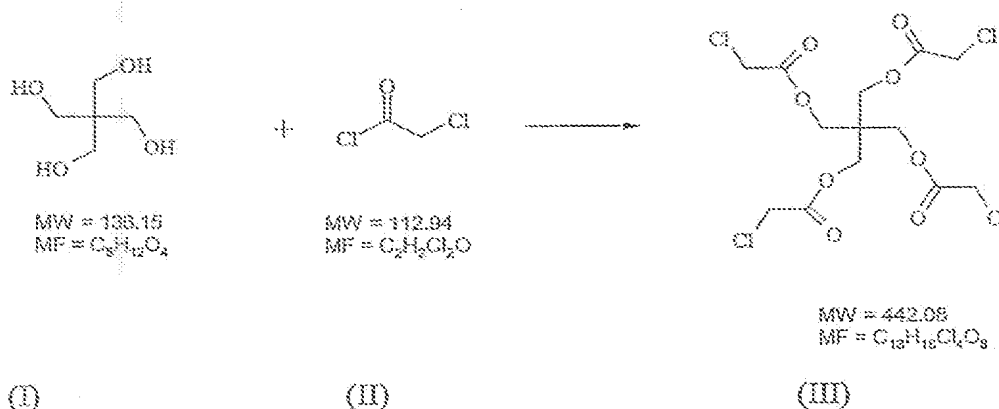
examples but several variations are possible within the spirit and scope of the invention.

## Examples

5

### Example 1

#### Production of tetrakis-(2-chloro-acetoxymethyl)-methane (Step 1)



10

Pentaerythritol (3.08 g, 22.6 mmol) was refluxed with chloroacetyl chloride (15.3 g, 136 mmol) for 45 minutes. Excess of acid chloride was removed in vacuo. The residue solidified on cooling and it was recrystallized twice from ethanol to give white flakes. The yield of tetrakis-(2-chloro-acetoxymethyl)-methane was 8.3 g (83 %).

$^1\text{H}$  ( $\text{CDCl}_3$ , 250 MHz)  $\delta_{\text{ppm}}$ : 4.08 (s, 8H, C- $\text{CH}_2$ ), 4.28 (s, 8H, - $\text{CH}_2$ -Cl)  
 $^{13}\text{C}$  ( $\text{CDCl}_3$ , 63 MHz)  $\delta_{\text{ppm}}$ : 40.45 ( $\text{CH}_2$ -Cl), 42.60 (C), 63.32 (C- $\text{CH}_2$ ), 166.66 (C=O)

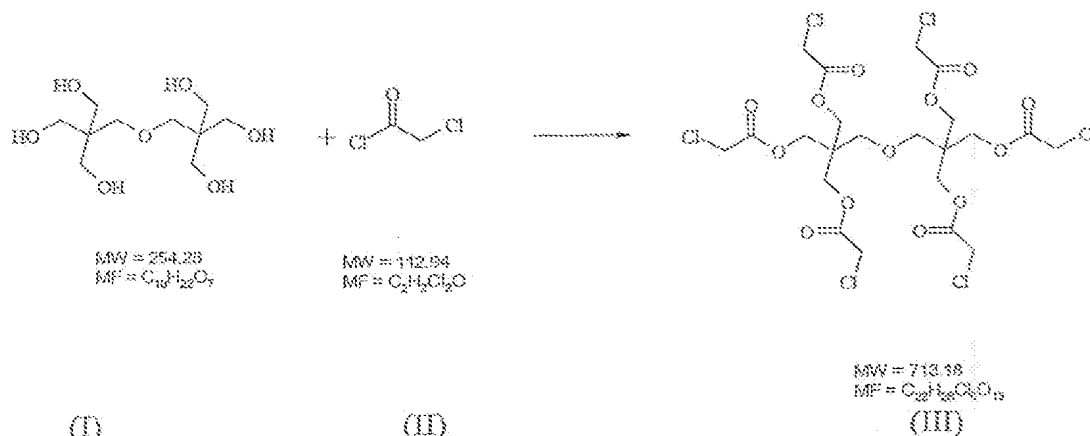
ESI-TOF-MS:  $m/z$  calc.  $\text{C}_{13}\text{H}_{16}\text{Cl}_4\text{O}_8$  442.08  $[\text{M}]^+$ , obtained 464.90  $[\text{M} + \text{Na}]^+$   
 m.p. = 95.9 °C

X-ray crystal structure of tetrakis-(2-chloro-acetoxymethyl)-methane is presented in figure 1.

25

## Example 2

## Production of 2,2,2-tris-(2-chloro-acetoxymethyl)-ethoxymethyl-tris-(2-chloro-acetoxymethyl)methane (Step 1)



Dipentaerythritol (7.13 g, 28.0 mmol) was refluxed with chloroacetyl chloride (25.5 g, 252 mmol) for 2 hours. Excess of acid chloride was removed in vacuo. The residue solidified on cooling and it was recrystallized twice from ethanol to give white flakes. The yield of 2,2,2-tris-(2-chloro-acetoxymethyl)-ethoxymethyl-tris-(2-chloro-acetoxymethyl)methane was 14.2 g (71 %).

<sup>1</sup>H (CDCl<sub>3</sub>, 250 MHz) δ<sub>ppm</sub>: 3.41 (s, 4H, O-CH<sub>2</sub>), 4.23 (s, 12H, -CH<sub>2</sub>-Cl), 4.42 (s, 12H, C-CH<sub>2</sub>)

<sup>13</sup>C (CDCl<sub>3</sub>, 63 MHz) δ<sub>ppm</sub>: 42.83 (C), 45.68 (CH<sub>2</sub>-Cl), 61.09 (C-CH<sub>2</sub>), 70.88 (O-CH<sub>2</sub> C), 166.99 (C=O)

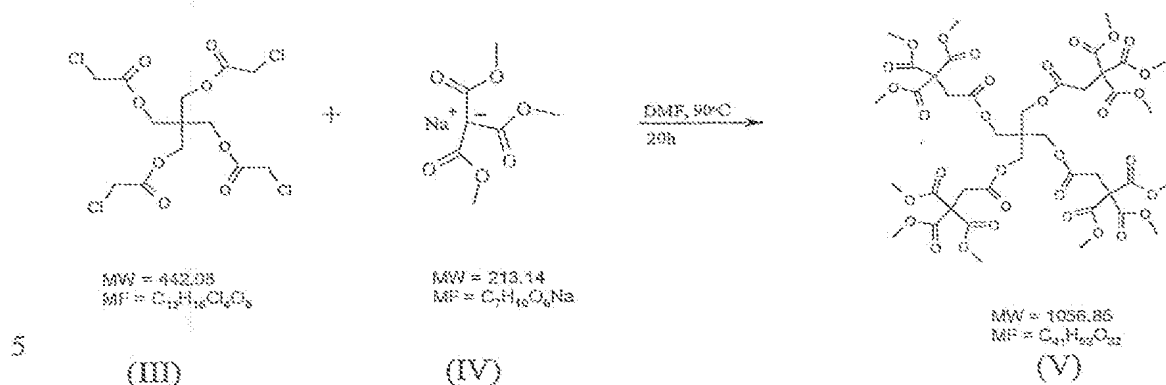
ESI-TOF-MS: *m/z* calc. C<sub>22</sub>H<sub>28</sub>Cl<sub>6</sub>O<sub>13</sub> 713.18 [M]<sup>+</sup>, obtained 732.97 [M + Na]<sup>+</sup>

m.p. = 212.8 °C

X-ray crystal structure of 2,2,2-tris-(2-chloro-acetoxymethyl)-ethoxymethyl-tris-(2-chloro-acetoxymethyl)methane is presented in figure 2.

## Example 3

## Production of tetrakis-(2,2,2-tris-(methoxycarbonyl)-acetoxymethyl)-methane (Step 2)



Tetrakis-(2-chloro-acetoxymethyl)-methane, obtained in example 1 (1.27 g, 2.88 mmol) was added to a stirred solution of  $\text{NaC}(\text{CO}_2\text{Me})_3$  (2.70 g, 12.7 mmol) in DMF (40 ml) at 90 °C. After 20 hours, the solution was cooled down to RT and  $\text{CHCl}_3$  (75 ml) was added. The solution was washed with water (3\*30ml), saturated  $\text{NaHCO}_3$  (3\*30 ml), water (3\*30ml), and dried over anhydrous  $\text{MgSO}_4$ . The solution was concentrated in vacuo, then ethanol was added. The product was crystallized as white flakes. The yield of tetrakis-(2,2,2-tris-(methoxycarbonyl)-acetoxymethyl)-methane was 2.8 g (93 %).

$^1\text{H}$  ( $\text{CDCl}_3$ , 250 MHz)  $\delta_{\text{ppm}}$ : 3.09 (s, 8H,  $\text{CO}-\text{CH}_2-\text{C}$ ), 3.73 (s, 36H,  $\text{O}-\text{CH}_3$ ), 4.08 (s, 8H,  $\text{C}-\text{CH}_2-\text{O}$ )

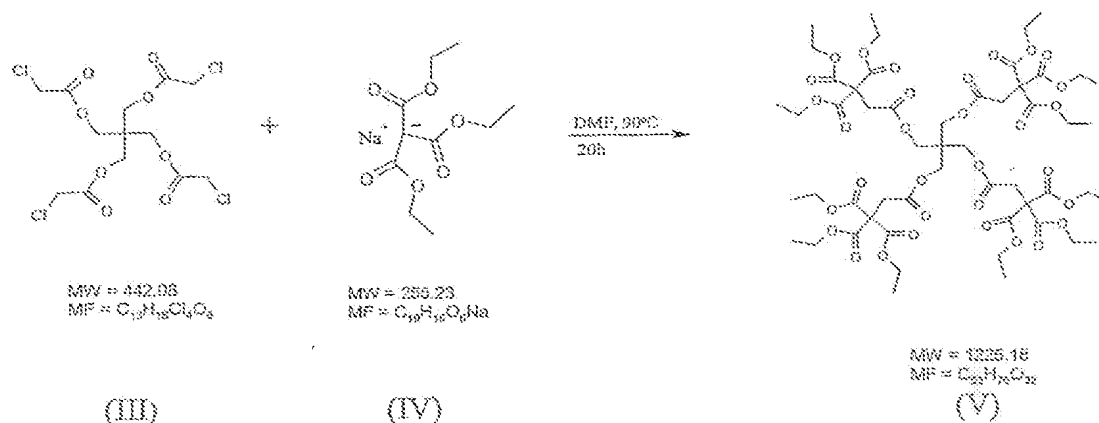
$^{13}\text{C}$  ( $\text{CDCl}_3$ , 63 MHz)  $\delta_{\text{ppm}}$ : 37.06 ( $\text{CO}-\text{CH}_2-\text{C}$ ), 41.45 ( $\text{C}-\text{CH}_2$ ), 53.47 ( $\text{O}-\text{CH}_3$ ), 62.60 ( $\text{CH}_2-\text{C}-\text{CO}$ ) 62.90 ( $\text{C}-\text{CH}_2-\text{O}$ ) 166.04 ( $\text{C}-\text{C}=\text{O}-\text{O}$ ), 168.85 ( $\text{O}-\text{C}=\text{O}-\text{CH}_2$ )

ESI-TOF-MS:  $m/z$  calc.  $\text{C}_{41}\text{H}_{52}\text{O}_{32}$  1056.85  $[\text{M}]^+$ , obtained 1057.23  $[\text{M} + 1]^+$ , 1079.22  $[\text{M} + \text{Na}]^+$ , 1095.20  $[\text{M} + \text{K}]^+$

m.p. = 154.4 °C

X-ray crystal structure of tetrakis-(2,2,2-tris-(methoxycarbonyl)-acetoxymethyl)methane is presented in figure 3.

## Example 4

Production of tetrakis-(2,2,2-tris-(ethoxycarbonyl)-acetoxymethyl)methane  
(Step 2)

Tetrakis-(2-chloro-acetoxymethyl)-methane, obtained in example 1 (1.44 g, 3.26 mmol) was added to a stirred solution of  $\text{NaC}(\text{CO}_2\text{Et})_3$  (3.33 g, 13.1 mmol) in DMF (40 ml) at 90 °C. After 20 hours, the solution was cooled down to RT and  $\text{CHCl}_3$  (75 ml) was added. The solution was washed with water (3\*30ml), saturated  $\text{NaHCO}_3$  (3\*30 ml), water (3\*30ml), and dried over anhydrous  $\text{MgSO}_4$ . The solution was concentrated in vacuo, then ethanol was added. The product crystallized as white flakes. The yield of tetrakis-(2,2,2-tris-(ethoxycarbonyl)-acetoxymethyl)methane was 3.13 g (79 %).

$^1\text{H}$  ( $\text{CDCl}_3$ , 250 MHz)  $\delta_{\text{ppm}}$ : 1.28 (t, 36H,  $\text{O}-\text{CH}_2-\text{CH}_3$ ), 3.14 (s, 8H,  $\text{CO}-\text{CH}_2-\text{C}$ ), 4.18 (s, 8H,  $\text{C}-\text{CH}_2-\text{O}$ ), 4.27 (q, 24H,  $\text{O}-\text{CH}_2-\text{CH}_3$ )

$^{13}\text{C}$  ( $\text{CDCl}_3$ , 63 MHz)  $\delta_{\text{ppm}}$ : 13.64 ( $\text{CH}_2-\text{CH}_3$ ), 36.93 ( $\text{CO}-\text{CH}_2-\text{C}$ ), 41.44 ( $\text{C}-\text{CH}_2$ ), 62.42 ( $\text{O}-\text{CH}_2-\text{CH}_3$ ), 62.97 ( $\text{C}-\text{CO}$ ), 63.26 ( $\text{C}-\text{CH}_2-\text{O}$ ), 165.67 ( $\text{C}-\text{C}=\text{O}-\text{O}$ ), 168.96 ( $\text{O}-\text{C}=\text{O}-\text{CH}_2$ )

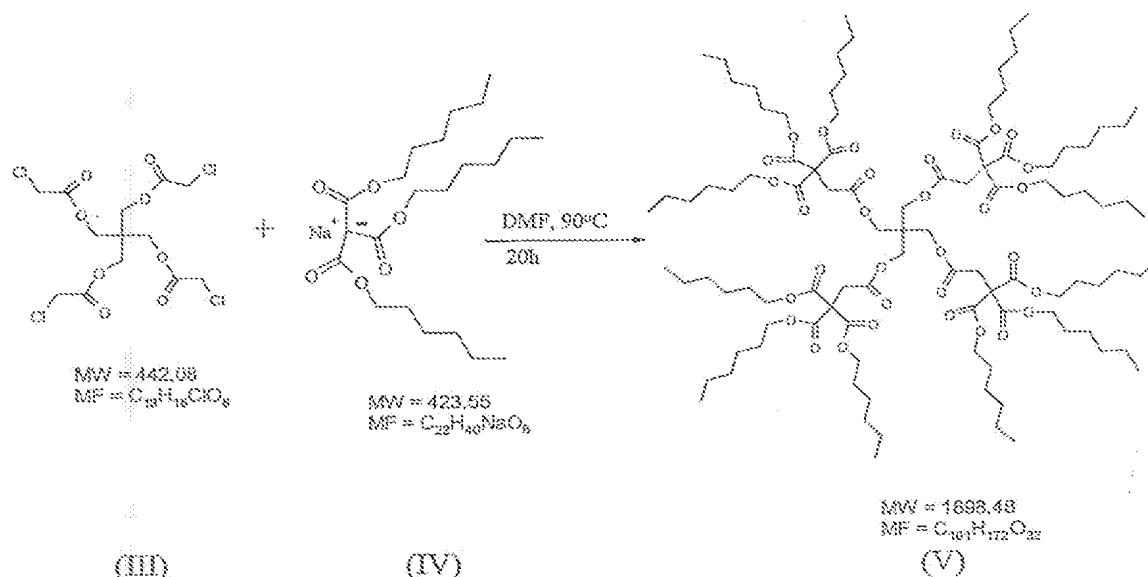
ESI-TOF-MS:  $m/z$  calc.  $\text{C}_{53}\text{H}_{76}\text{O}_{32}$  1225.18  $[\text{M}]^+$  obtained 1225.44  $[\text{M}+1]^+$ , 1247.43  $[\text{M}+\text{Na}]^+$ , 1263.40  $[\text{M}+\text{K}]^+$

m.p. = 110.8 °C

X-ray crystal structure of tetrakis-(2,2,2-tris-(ethoxycarbonyl)-acetoxymethyl)methane is presented in figure 4.

## Example 5

## Production of dodecahexyl polyester dendrimer (Step 2)



Tetrakis-(2-chloro-acetoxymethyl)-methane, obtained in example 1 (1.78 g, 4.03 mmol) was added to a stirred solution of  $\text{NaC}(\text{CO}_2\text{Hex})_3$  (6.83 g, 16.1 mmol) in DMF (40 ml) at 90 °C. After 20 hours, the solution was cooled down to RT and  $\text{CHCl}_3$  (75 ml) was added. The solution was washed with water (3\*30ml), saturated  $\text{NaHCO}_3$  (3\*30 ml), water (3\*30ml), and dried over anhydrous  $\text{MgSO}_4$ . The solution was concentrated in vacuo. The product dodecahexyl polyester dendrimer was dark oil. Yield 4.03 g (13 %).

$^1\text{H}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta_{\text{ppm}}$ : 0.85 (t, 36H,  $-\text{CH}_3$ ), 1.26 (m, 72H,  $-\text{CH}_2$ ), 1.60 (m, 24H,  $-\text{CH}_2$ ), 3.10 (s, 8H,  $-\text{CH}_2$ ), 4.01 – 4.16 (m, 32H,  $\text{OCH}_2 + \text{CH}_2$ )

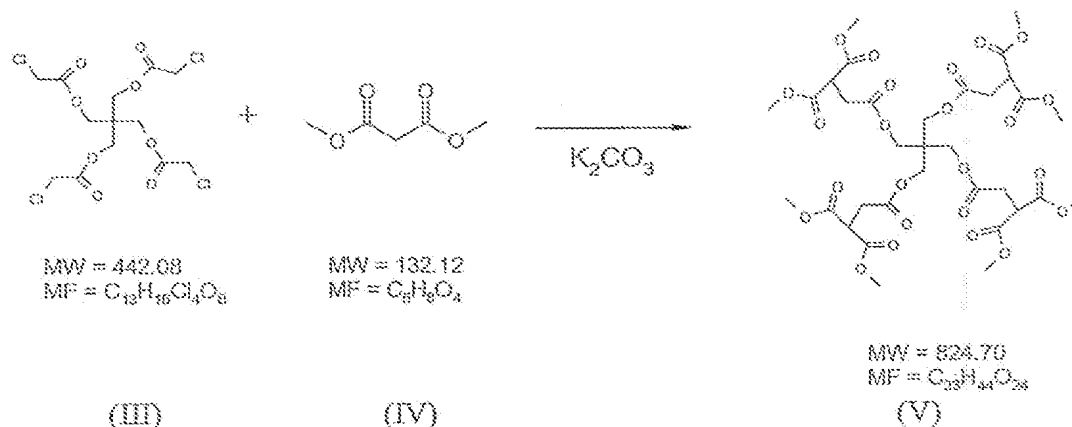
$^{13}\text{C}$  ( $\text{CDCl}_3$ , 123 MHz)  $\delta_{\text{ppm}}$ : 13.80 ( $\text{CH}_3$ ), 22.37 ( $\text{CH}_2$ ), 25.27 ( $\text{CH}_2$ ), 28.16 ( $\text{CH}_2$ ), 31.22 ( $\text{CH}_2$ ), 41.57 ( $\text{CO}-\text{CH}_2$ ), 47.83 (C), 65.78 ( $\text{OCH}_2$ ), 65.96 (C), 66.51 ( $\text{CH}_2\text{O}$ ), 166.04 ( $\text{C}=\text{O}$ ), 168.35 ( $\text{C}=\text{O}$ )

ESI-TOF-MS:  $m/z$  calcd for  $\text{C}_{101}\text{H}_{172}\text{O}_{32}$  1898.48  $[\text{M}]^+$ , found 1898.06  $[\text{M}]^+$



## Example 6

## Production of octamethyl polyester dendrimer (Step 2)



5

A mixture of tetrakis-(2-chloro-acetoxymethyl)-methane, obtained in example 1 (0.88 g, 2.00 mmol), dimethyl malonate (1.11 g, 8.40 mmol) and  $K_2CO_3$  (1.16 g) in DMF (10 ml) was stirred at 25 °C for 24 hours. The mixture was filtered, and the solid was washed with DMF (10 ml). The combined filtrate was concentrated to give a residue, which was dissolved in  $CHCl_3$  (75 ml), then washed with water (2\*30 ml), 15 % NaOH (2\*30 ml), and water 2\*30 ml), dried over anhydrous  $MgSO_4$ , and concentrated in vacuo. To the residue methanol was added and the product precipitated. After filtration and drying in vacuo 1.2 g (70 %) of the product octamethyl polyester dendrimer was obtained.

15

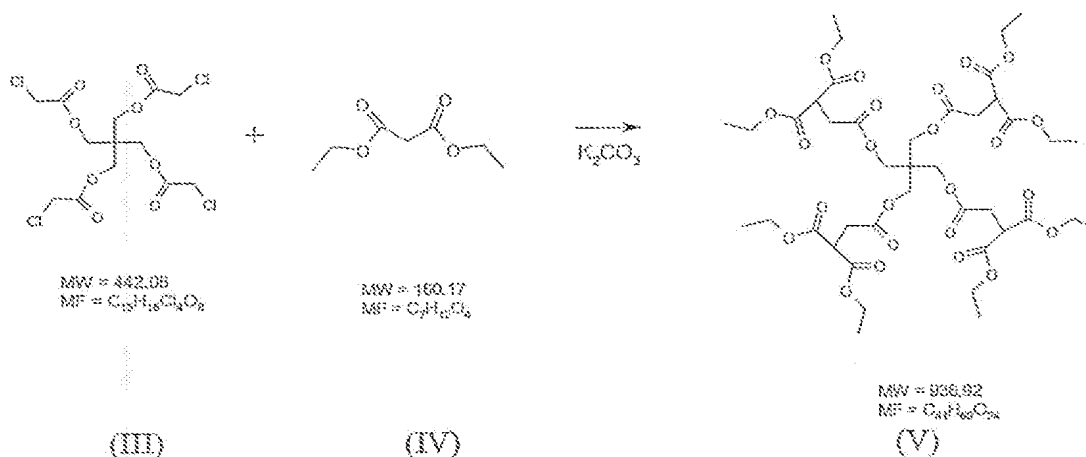
$^1H$  ( $CDCl_3$ , 500 MHz, -30°C)  $\delta_{ppm}$ : 3.38 (s, 8H, C- $CH_2$ ), 3.41 (s, 24H, - $CH_3$ ), 3.73 (d, 8H,  $CH_2$ -CH) 4.05-4.10 (m, 4H,  $CH_2$ -CH)

$^{13}C$  ( $CDCl_3$ , 126 MHz)  $\delta_{ppm}$ : 32.89 ( $CH_2$ -CH), 42.12 (C), 47.31 ( $CH_2$ -CH), 50.64 ( $CH_3$ ), 52.97 (C- $CH_2$ ), 168.52 (CH-C=O), 169.87 (O-C=O- $CH_2$ )

20

## Example 7

## Production of octaethyl polyester dendrimer (Step 2)



5

A mixture of tetrakis-(2-chloro-acetoxymethyl)-methane, obtained in example 1 (2.36 g, 5.34 mmol), diethyl malonate (3.42 g, 21.3 mmol) and  $K_2CO_3$  (2.95 g) in DMF (10 ml) was stirred at 25 °C for 24 h. The mixture was filtered, and the solid was washed with DMF (10 ml). The combined filtrate was concentrated to give a residue, which was dissolved in  $CHCl_3$  (75 ml), washed with water (2\*30 ml), 15 % NaOH (2\*30 ml), water (2\*30 ml), dried over anhydrous  $MgSO_4$ , concentrated in vacuo. To the residue methanol was added and product precipitated. After filtration and drying in vacuo 3.5 g (70 %) of product octaethyl polyester dendrimer was obtained.

15

$^1H$  ( $CDCl_3$ , 250 MHz)  $\delta_{ppm}$ : 1.27 (t, 24H,  $-CH_3$ ), 2.92 (d, 8H,  $CO-CH_2-CH$ ), 3.80 (t, 4H,  $CH_2-CH$ ), 4.05 - 4.28 (m, 24H,  $O-CH_2-CH_3$  and  $C-CH_2$ )

$^{13}C$  ( $CDCl_3$ , 63 MHz)  $\delta_{ppm}$ : 13.95 ( $CH_3$ ) 32.85 ( $CO-CH_2-CH$ ), 42.06 ( $C-CH_2$ ), 47.71 ( $CH$ ), 61.44 ( $CH_2-CH_3$ ) 61.79 ( $C-CH_2-O$ ) 170.23 ( $CH-C=O$ ), 168.13 ( $O-C=O-CH_2$ )

20

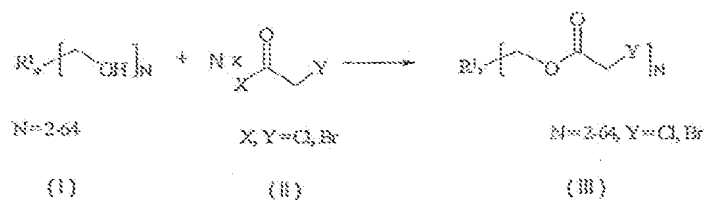
ESI-TOF-MS:  $m/z$  calc.  $C_{41}H_{60}O_{24}$  936.92  $[M]^+$ , obtained 937.30  $[M+1]^+$ , 959.27  $[M+Na]^+$ , 975.29  $[M+K]^+$

## Claims

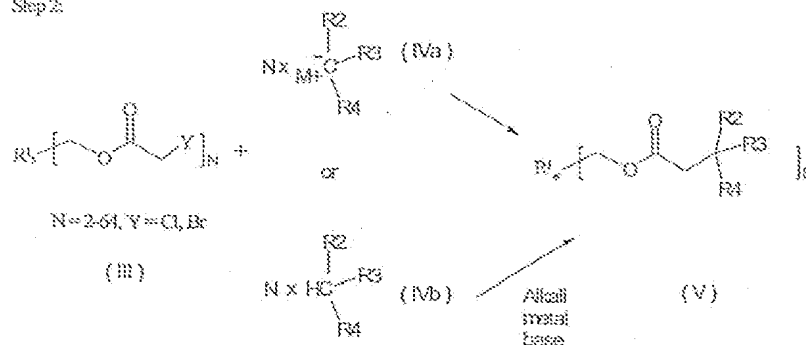
1. Polyester dendrimers of a polyol with 2-64 reactive hydroxyl groups wherein the surface of the dendrimers is formed using an alternating sequence of haloacetyl halide and an alkali metal enolate.
2. Polyester dendrimers according to claim 1, characterized in that said dendrimers are methyl and ethyl functionalised bis- and tris-carboxylates.
3. Polyester dendrimers according to claim 1 or 2, characterized in that said dendrimers are single crystal forming crystalline compounds or liquid compounds.
4. A method for the manufacture of polyester dendrimers, characterized in that the method comprises steps 1 and 2, wherein:

## SCHEME 1

Step 1:



Step 2:



- in step 1, a polyol (I), where N is 2 - 64 and  $R^1$  is an unsubstituted or substituted aliphatic group selected from the group consisting of linear or branched alkyl groups containing 1-100 carbon atoms, linear or branched alkenyl and alkynyl groups containing 2-100 carbon atoms, or a (hetero) aromatic group selected from the group consisting of 1,n-dihydroxybenzene, where n is 2,3 or 4, 1,n,y-trihydroxybenzene, where n is 2,3 or 4 and y is 3,4,5 or 6, is allowed to react with a haloacetyl halide (II) and, after optional recrystallization from a solvent or a mixture of solvents, a polyester polyhalide (III) is obtained; and
- in step 2, the obtained polyester polyhalide (III) is allowed to react with an alkali metal enolate (IVa), or bis- or tris(carbonyl)methane compound (IVb) together with an alkali metal base, where the groups  $R^2$ ,  $R^3$  and  $R^4$  are selected, independently from each other, from a group consisting of H, COH, CSH, COOR<sup>5</sup>, COSR<sup>5</sup>, CSOR<sup>5</sup>, CSSR<sup>5</sup>, COR<sup>5</sup>, CSR<sup>5</sup>, CONR<sup>5</sup>R<sup>6</sup>, CSNR<sup>5</sup>R<sup>6</sup>, wherein the groups  $R^5$  and  $R^6$  are selected independently from each other, from a group consisting of H, linear and branched alkyl groups containing 1-100 carbon atoms, linear and branched alkenyl or alkynyl groups containing 2-100 carbon atoms, aryl groups, (hetero) aromatic groups and aliphatic heterocyclic groups, which contain oxygen, sulfur, nitrogen or phosphorous atoms, in a solvent and at an elevated temperature, and the product polyester dendrimer (V) is optionally purified.

5. A method according to claim 4, characterized in that in the polyol (I) N is 2-20 and preferably 3-12.

6. A method according to claim 4, characterized in that the polyol (I) is pentaerythritol or dipentaerythritol.

7. A method according to claim 4, characterized in that the group  $R^1$  is an unsubstituted or substituted aliphatic group selected from the group consisting of linear

or branched alkyl groups containing 1–20 and preferably 1–10 carbon atoms, linear or branched alkenyl and alkynyl groups containing 2–20 and preferably 2–10 carbon atoms, or a 1,3,5-trihydroxybenzene group.

5 8. A method according to claim 7, **characterized** in that the group  $R^1$  is a methyl, ethyl, propyl, isobutyl or butyl group.

9. A method according to claim 4, **characterized** in that the groups  $R^5$  and  $R^6$  are selected, independently from each other, from a group consisting of linear and  
10 branched alkyl groups containing 1–20 and preferably 1–10 carbon atoms, linear and branched alkenyl or alkynyl groups containing 2–20 and preferably 2–10 carbon atoms and optionally the aliphatic group is substituted with (hetero) aliphatic or (hetero) aromatic groups.

15 10. A method according to claim 4, **characterized** in that the groups  $R^5$  and  $R^6$  are selected, independently from each other, from methyl, ethyl, propyl, isobutyl, butyl, 3-hydroxymethylpyridine, 2-hydroxymethylthiophene, 2-hydroxymethylfuran, 2-hydroxymethylpyrrole and hydroxymethyldiethyl phosphonate groups.

20 11. A method according to claim 4, **characterized** in that the haloacetyl halide (II) it is chloroacetyl chloride, bromoacetyl bromide or bromoacetyl chloride.

12. A method according to claim 4, **characterized** in that groups  $R^2$ ,  $R^3$  and  $R^4$  are selected, independently from each other, from methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and hexyloxycarbonyl groups.  
25

13. A method according to claim 4, **characterized** in that the alkali metal enolate is an alkali metal enolate of functionalized bis- or tris(carbonyl)methane compound (IVa), or a functionalized bis- or tris(carbonyl)methane compound (IVb)  
30 together with an alkali metal base.

14. A method according to claim 4, **characterized** in that the compound (IVa) is  $\text{NaC}(\text{CO}_2\text{Me})_3$  or  $\text{NaC}(\text{CO}_2\text{Et})_3$ , or the compound (IVb) together with an alkali metal base are  $\text{H}_2\text{C}(\text{CO}_2\text{Me})_2$  or  $\text{H}_2\text{C}(\text{CO}_2\text{Et})_2$  together with  $\text{K}_2\text{CO}_3$ .

- 5 15. A method according to claim 4, **characterized** in that in step 1, 1–50 mol of haloacetyl halide (II) per hydroxyl group is allowed to react with a polyol (I), at a temperature of 20–150 °C and the reaction mixture is refluxed until gaseous acid formation is ceased, then the excess of haloacetyl halide (II) is removed by evaporation and the solid intermediate (III) obtained is separated.

10

16. A method according to claim 4 or 15, **characterized** in that in step 1, 1–5 mol of haloacetyl halide (II) per hydroxyl group is reacted with a polyol (I) at 60–150 °C and the reaction mixture is refluxed until gaseous acid formation is ceased, then the excess of haloacetyl halide (II) is removed by evaporation under vacuum and the solid intermediate (III) obtained is filtered and dried and optionally the intermediate (III) is recrystallized from a solvent or a mixture of solvents.

15

17. A method according to claim 4, **characterized** in that in step 2, the intermediate (III) obtained from step 1 is allowed to react with an alkali metal enolate (IVa), or bis/tris(carbonyl)methane compound (IVb) together with an alkali metal base, in an inert aprotic solvent or a mixture of inert aprotic solvents, at a temperature of 20–120 °C, the reaction mixture is then agitated at a temperature of 20–120 °C and it is then cooled, a non-polar solvent or a mixture of non-polar solvents is added to the reaction mixture, and the obtained mixture is then washed, dried and the solvent is evaporated, a polar solvent or a mixture of polar solvents is added and the obtained final product dendrimer (V) is separated.

20

18. A method according to claim 4 or 17, **characterized** in that in step 2, the intermediate (III) obtained from step 1 is reacted with an alkali metal enolate (IVa), or bis or tris(carbonyl)methane compound (IVb) together with an alkali metal

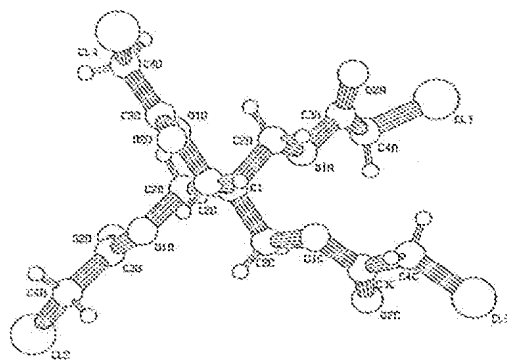
30

base, in DMF, at 60–100 °C, the reaction mixture is then agitated at a temperature of 80–100 °C and it is then cooled to room temperature, chloroform is added to the reaction mixture, and the obtained mixture is then washed, dried and the solvent is evaporated under vacuum an alcohol is added and the obtained final product dendrimer (V) is separated.

19. The polyester dendrimers according to any one claims 1-3, characterized in that they are obtainable according to the method of any one of claims 4-18.

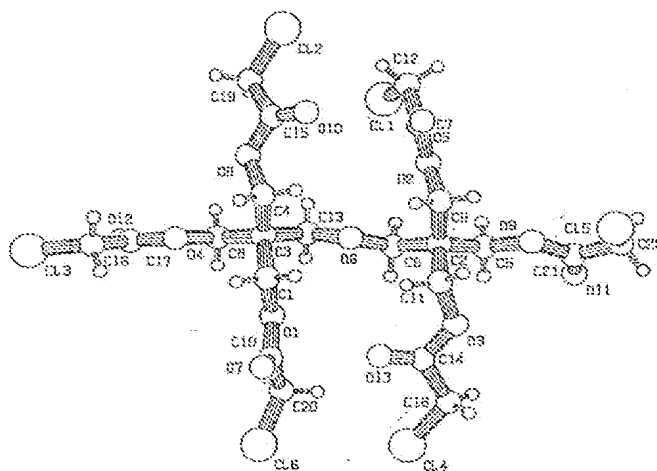
20. Use of polyester dendrimers according to any one of claim 1–3 and 19 or manufactured according to any one of claims 4–18, as catalysts, parts of pharmaceuticals, carriers, transporters, imaging agents in medicine, in improving viscosity or general properties of cosmetics, as glues and coating agents, matrix material for inorganic or organic or bio-composites, lubricants, anti-corrosion agents, pesticides or agricultural chemicals, polyfunctional cross linkers in polymer and gel production, medical and dentistry preparates, dentures and prosthesis and ion-selective complexation agents for analytical and catalysis applications.

1/2



X-ray crystal structure of tetrakis-(2-chloro-acetoxymethyl)-methane

FIG. 1

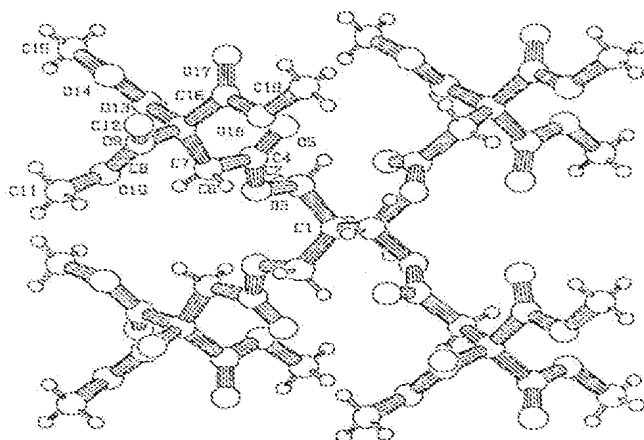


X-ray crystal structure of 2,2,2-tris-(2-chloro-acetoxy-methyl)-ethoxymethyl-tris-(2-chloro-acetoxymethyl)methane

FIG. 2

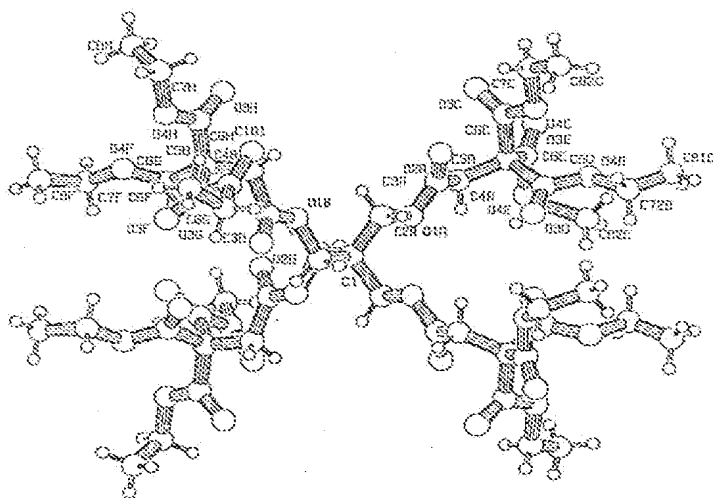


2/2



X-ray crystal structure of tetrakis-(2,2,2-tris-(methoxycarbonyl)-  
acetoxymethyl)methane

FIG. 3



X-ray crystal structure of tetrakis-(2,2,2-tris-(ethoxycarbonyl)-  
acetoxymethyl)methane

FIG. 4

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/FI 03/00074

## A. CLASSIFICATION OF SUBJECT MATTER

IPC7: C08G 83/00, C08G 85/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: C08G, C08L, C09D, C09J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-INTERNAL, WPI DATA, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 0196291 A1 (NATIONAL STARCH AND CHEMICAL INVESTMENT HOLDINGS CORPORATION), 20 December 2001 (20.12.01)	1-20
A	WO 9208749 A1 (CORNELL RESEARCH FOUNDATION, INC.), 29 May 1992 (29.05.92)	1-20
A	EP 1006101 A1 (NIPPON STEEL CHEMICAL CO., LTD.), 7 June 2000 (07.06.00)	1-20
A	US 5834118 A (BENGT RANBY ET AL), 10 November 1998 (10.11.98)	1-20

☒ Further documents are listed in the continuation of Box C.☒ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

22 April 2003

Date of mailing of the international search report

29-04-2003

Name and mailing address of the ISA/

Swedish Patent Office

Box 5055, S-102 42 STOCKHOLM

Facsimile No. +46 8 666 02 86

Authorized officer

Johanna Brolund/EÖ

Telephone No. +46 8 782 25 00

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/FI 03/00074

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5418301 A (ANDERS HULT ET AL), 23 May 1995 (23.05.95)  -----	1-20

## INTERNATIONAL SEARCH REPORT

Information on patent family members

29/03/03

International application No.

PCT/FI 03/00074

Patent document cited in search report			Publication date	Patent family member(s)		Publication date
WO	0196291	A1	20/12/01	AU	5456500 A	24/12/01
				EP	1289946 A	12/03/03
WO	9208749	A1	29/05/92	AT	152147 T	15/05/97
				CA	2096144 A	20/05/92
				DE	69125846 D,T	27/11/97
				EP	0558556 A,B	08/09/93
				JP	2795418 B	10/09/98
				JP	6502442 T	17/03/94
				US	5514764 A	07/05/96
				US	6300424 B	09/10/01
EP	1006101	A1	07/06/00	US	6255444 B	03/07/01
				JP	11060540 A	02/03/99
				WO	9908993 A	25/02/99
US	5834118	A	10/11/98	AT	187467 T	15/12/99
				AU	704344 B	22/04/99
				AU	3489395 A	27/03/96
				CA	2198755 A	14/03/96
				CN	1070878 B	12/09/01
				CN	1163626 A	29/10/97
				DE	69513840 D,T	27/07/00
				DK	779908 T	08/05/00
				EP	0779908 A,B	25/06/97
				SE	0779908 T3	
				ES	2140704 T	01/03/00
				GR	3032356 T	27/04/00
				JP	10505377 T	26/05/98
				NO	311300 B	12/11/01
				NO	971061 A	30/04/97
				PT	779908 T	31/05/00
				RU	2162861 C	10/02/01
				SE	503559 C	08/07/96
				SE	9402994 A	09/03/96
				WO	9607688 A	14/03/96

## INTERNATIONAL SEARCH REPORT

Information on patent family members

29/03/03

International application No.

PCT/FI 03/00074

Patent document cited in search report			Publication date	Patent family member(s)	Publication date
US	5418301	A	23/05/95	AT 165609 T	15/05/98
				AU 3653093 A	13/09/93
				CA 2117486 A,C	02/09/93
				DE 69214153 D,T	10/04/97
				DE 69318295 D,T	01/10/98
				DK 630389 T	07/10/98
				EP 0597042 A,B	18/05/94
				EP 0630389 A,B	28/12/94
				SE 0630389 T3	
				ES 2115762 T	01/07/98
				FI 931821 A	22/04/93
				HK 1005487 A	00/00/00
				JP 2574201 B	22/01/97
				JP 6507512 T	25/08/94
				JP 7504219 T	11/05/95
				KR 158912 B	15/01/99
				SE 468771 B,C	15/03/93
				SE 9200564 A	15/03/93
				US 5378886 A	03/01/95
				WO 9317060 A	02/09/93
				SE 9300148 A	21/07/94

